

43. The recombinant DNA sequence shown in Figure 2 (consisting of Figures 2a, 2b, 2c, 2d, 2e).

44. A complete GS-encoding recombinant DNA sequence from one mammalian species which hybridises under high stringency conditions with the recombinant DNA sequence of claim 39 or a part thereof from a different species.

45. The recombinant DNA sequence of claim 39, which is cDNA.

46. The recombinant DNA sequence of claim 45 wherein the cDNA is derived by reverse transcription.

47. The recombinant DNA sequence of claim 39, which comprises a fragment of genomic DNA.

48. Use of the recombinant DNA sequence of claim 39 as a hybridisation probe.

49. The recombinant DNA sequence of claim 39 for use in medical or diagnostic methods such as for detecting disease states in which the level of GS in a subject is altered.

50. A recombinant DNA vector comprising the recombinant DNA sequence of claim 39.

51. The vector of claim 50, which is an expression vector capable, in a transformant host cell, of expressing the recombinant DNA sequence which encodes the complete amino acid sequence of a mammalian glutamine synthetase (GS).

52. A recombinant DNA vector comprising a recombinant DNA sequence which encodes the complete amino acid sequence of a GS, further comprising a recombinant DNA sequence which encodes the complete amino acid sequence of a desired protein other than said GS.

53. A recombinant DNA vector comprising a recombinant DNA sequence which encodes the complete amino acid sequence of a GS, further comprising a recombinant DNA sequence which encodes the complete amino acid sequence of a desired protein other than said GS, the vector being capable, in a transformant host cell, of expressing the recombinant DNA sequence for the GS and for the desired protein.

54. The vector of claim 51, wherein the GS-encoding recombinant DNA sequence is under the control of a regulatable promoter.

55. The vector of claim 54, wherein the regulatable promoter is a heat shock promoter or a metallothionein promoter.

56. Plasmid pSVLGS.1.

57. Plasmid pSV2.GS.

58. Plasmid pZIPGS.

59. Plasmid pSVLGS.tPA16.

60. Plasmid pSVLGS.tPA17.

61. A host cell transformed with a vector according to claim 50.

62. A method for co-amplifying a recombinant DNA sequence which encodes the complete amino acid sequence of a desired protein other than GS, which comprises co-transforming a host cell with an expression vector capable, in a transformant host cell, of expressing a recombinant DNA sequence which encodes the complete amino acid sequence of a GS, and an

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expression vector comprising said desired protein recombinant DNA sequence.

63. A method for co-amplifying a recombinant DNA sequence which encodes the complete amino acid sequence of a desired protein other than GS which comprises transforming a host cell with a vector according to claim 53.

64. The method of claim 62, wherein the desired protein is tissue plasminogen activator.

65. The method of claim 62, wherein amplification is achieved by selection for resistance to progressively increased levels of a GS inhibitor.

66. The method of claim 65, wherein the GS inhibitor is phosphinothricin or methionine sulphoximine.

67. The method of claim 65, wherein after amplification, the level of GS accumulation is reduced by adding glutamine to the culture medium.

68. The method of claim 65, wherein the amount of GS inhibitor required to cause amplification is reduced by the addition of methionine to the culture medium.

69. The method of claim 62, wherein the GS-encoding recombinant DNA sequence expression is switched on during selection and amplification and is subsequently down-regulated.

70. Use of an expression vector capable, in a transformant host cell, of expressing a recombinant DNA sequence which encodes the complete amino acid sequence of a GS,

as a dominant selectable marker by transforming a host cell which contains an active GS gene with the vector, thereby conferring transformant cells with resistance to GS inhibitors.

71. Use of a vector according to claim 51 in endowing a cell line with the ability to survive in a medium lacking glutamine by transforming a host cell either completely lacking or reduced in GS activity with the vector.

72. The method of claim 62, wherein the host cell is a mammalian cell.

73. The method of claim 62, wherein the host cell is a CHO-K1 cell.

74. The method of claim 71, wherein the host cell is a myeloma cell.--

REMARKS

The above amendments have been made to substitute for the original claims a new set of claims, the latter being free of multiple claim dependency.

Also, the specification has been amended to refer to sub-Figures 2a, 2b, 2c, 2d, 2e.

There are 36 claims in the specification, as amended, 9 being independent claims, and a total of 16 excess claims over 20. The appropriate fee for the excess claims is also submitted herewith.